MCMR-RCQ-HR (70) 16 Nov 1998

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Approval Process for The Surgeon General (TSG) Sponsored Investigational New Drug (IND) Protocols Reviewed by or Submitted to the Human Subjects Research Review Board (HSRRB)

1. This information is provided to inform investigators, review committees, and Command staffs of the process of HSRRB review for protocols involving TSG-sponsored INDs. Enclosure 1 diagrams this process.

2. The following information is provided to augment the diagram.

a. The HSRRB convenes scheduled meetings on the second Wednesday of every month. The agenda order for the HSRRB is normally based on the date of protocol receipt by the Human Subjects Protection Division (HSPD).

b. To be included on the meeting agenda, complete protocol packets must be received no later than ten (10) working days prior to the meeting. Hard copy protocols should be submitted to:

Commanding General
U.S. Army Medical Research and Materiel Command
Deputy Chief of Staff for Regulatory Compliance and Quality
Human Subjects Protection Division, ATTN: MCMR-RCQ-HR
504 Scott Street
Fort Detrick, MD 21702-5012

Protocols may also be transmitted via electronic mail or facsimile. Facsimile versions of a protocol should be sent to 301-619-7803 (DSN 343). Protocols may be electronically mailed to the Chief, Human Subjects Protection Division (mrmchsrrb@ftdetrck-ccmail.army.mil). Additionally, the Regulatory Affairs Division (RAD) and the appropriate product manager should be provided with the protocol. Electronically mailed protocols should be sent as attached documents in read

only format. Preferred formats include Word® 7.0 or Adobe Acrobat® 3.0 files. Contact Ms. Higgins to determine if a different format is acceptable. Signature pages need to be mailed separately or scanned in as part of the Adobe pdf file.

3. The following documents are necessary for HSRRB review (incomplete protocol packets will not be reviewed by the HSRRB):

a. The research protocol (preferably in ICH format, see Enclosure 2), to include a list of references and all case report forms. A policy describing requirements for laboratory procedures is being staffed at this time. Instructions for including a laboratory annex as part of clinical research protocols will be included in that policy.

b. The informed consent document (DA Form 5303-R or equivalent);

c. A Food and Drug Administration (FDA) Form 1572 signed by the Principal Investigator and listing associate investigators with copies of respective curriculum vitae (to include the medical monitor);

d. The minutes of all committees necessary for review and approval of the protocol (e.g. human use, ethics, scientific, radiation control, etc.); and

e. The Laboratory/Institute Commander’s recommendation on the protocol.

4. Investigators may submit draft protocols to the HSPD or RAD as appropriate for informal review prior to formal submission.

5. As indicated in the diagram, investigators must coordinate with the appropriate product manager at the U.S. Army Medical Materiel Development Activity (USAMMDA) or the Joint Vaccine Acquisition Program.

6. The USAMMDA Quality Assurance Division is required to conduct a pre-study visit before initiation of the protocol.

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7. The HSRRB and local human use committee (HUC) files are subject to FDA inspection. Therefore, updates or modifications to protocols must be submitted to the local HUC for appropriate action. These changes are then forwarded through the product manager to the Deputy Chief of Staff for Regulatory Compliance and Quality for submission to the FDA and for inclusion in the official IND files maintained by the Regulatory Affairs Division.

FOR THE COMMANDER:

2 Encl

CLAUDIA BARTZ
COL, AN
Acting Chairperson
Human Subjects Research Review Board

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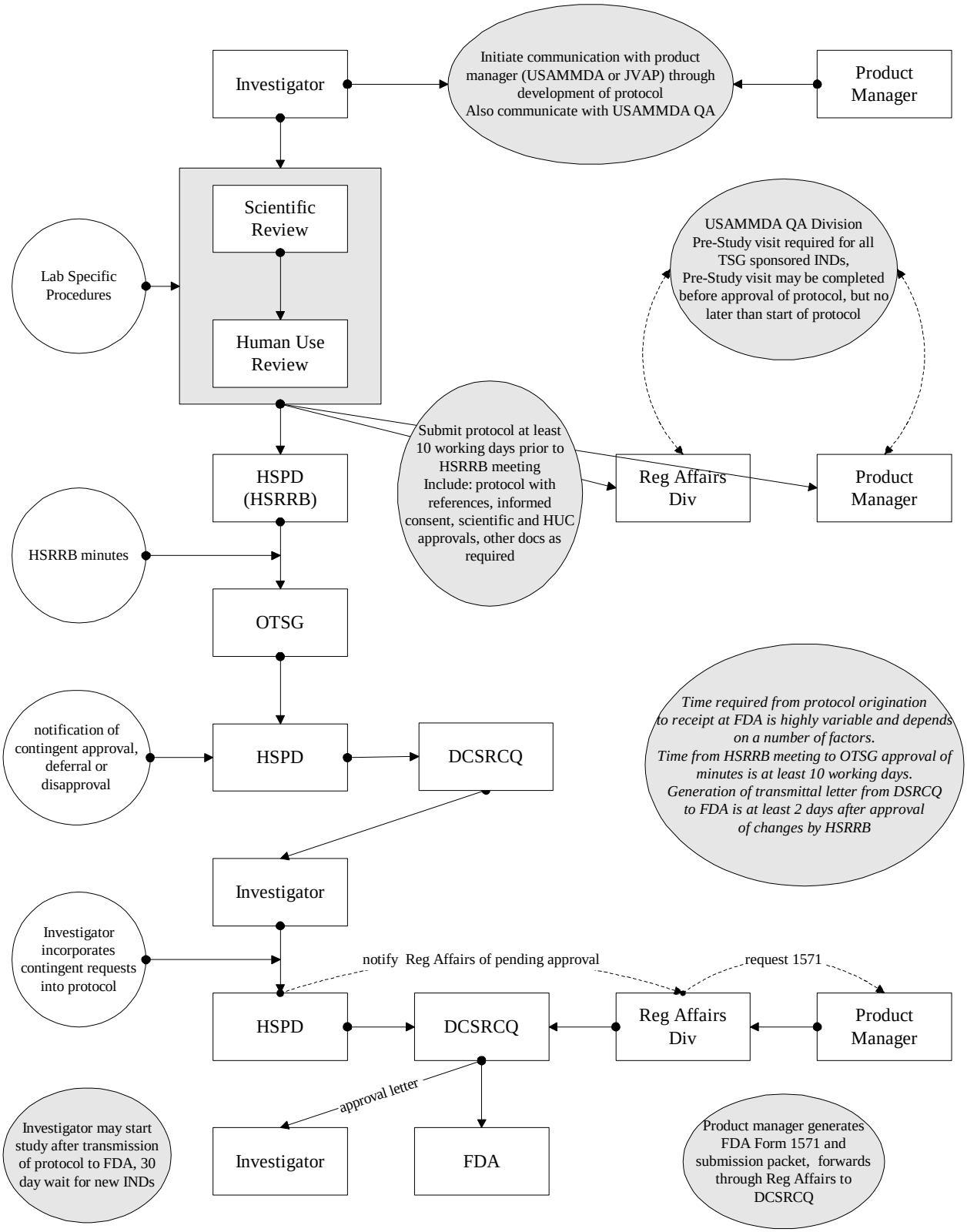
TSG-sponsored IND protocol approval process

(Does not include military contingency protocols)



Enclosure 1

6. CLINICAL TRIAL PROTOCOL AND PROTOCOL AMENDMENT(S)

The contents of a trial protocol should generally include the following topics. However, site specific information may be provided on separate protocol page(s), or addressed in a separate agreement, and some of the information listed below may be contained in other protocol referenced documents, such as an Investigator's Brochure.

6.1 General Information

6.1.1 Protocol title, protocol identifying number, and date. Any amendment(s) should also bear the amendment number(s) and date(s).

6.1.2 Name and address of the sponsor and monitor (if other than the sponsor).

6.1.3 Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.

6.1.4 Name, title, address, and telephone number(s) of the sponsor's medical expert (or dentist when appropriate) for the trial.

6.1.5 Name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).

6.1.6 Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than investigator).

6.1.7 Name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

6.2 Background Information

6.2.1 Name and description of the investigational product(s).

6.2.2 A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.

6.2.3 Summary of the known and potential risks and benefits, if any, to human subjects.

6.2.4 Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).

6.2.5 A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).

6.2.6 Description of the population to be studied.

6.2.7 References to literature and data that are relevant to the trial, and that provide background for the trial.

6.3 Trial Objectives and Purpose

A detailed description of the objectives and the purpose of the trial.

6.4 Trial Design

The scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design, should include:

6.4.1 A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.

6.4.2 A description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.

6.4.3 A description of the measures taken to minimize/avoid bias, including:

Guideline for Good Clinical Practice, May 9, 1997 (continued)

(a) Randomization.

(b) Blinding.

6.4.4 A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s).

6.4.5 The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.

6.4.6 A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

6.4.7 Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.

6.4.8 Maintenance of trial treatment randomization codes and procedures for breaking codes.

6.4.9 The identification of any data to be recorded directly on the CRFs (i.e. no prior written or electronic record of data), and to be considered to be source data.

6.5 Selection and Withdrawal of Subjects

6.5.1 Subject inclusion criteria.

6.5.2 Subject exclusion criteria.

6.5.3 Subject withdrawal criteria (i.e. terminating investigational product treatment/trial treatment) and procedures specifying:

(a) When and how to withdraw subjects from the trial/ investigational product treatment.

(b) The type and timing of the data to be collected for withdrawn subjects.

(c) Whether and how subjects are to be replaced.

(d) The follow-up for subjects withdrawn from investigational product treatment/trial treatment.

6.6 Treatment of Subjects

6.6.1 The treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of

administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.

6.6.2 Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.

6.6.3 Procedures for monitoring subject compliance.

6.7 Assessment of Efficacy

6.7.1 Specification of the efficacy parameters.

6.7.2 Methods and timing for assessing, recording, and analysing of efficacy parameters.

6.8 Assessment of Safety

6.8.1 Specification of safety parameters.

6.8.2 The methods and timing for assessing, recording, and analysing safety parameters.

6.8.3 Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.

6.8.4 The type and duration of the follow-up of subjects after adverse events.

6.9 Statistics

6.9.1 A description of the statistical methods to be employed, including timing of any planned interim analysis(ses).

6.9.2 The number of subjects planned to be enrolled. In multicentre trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.

6.9.3 The level of significance to be used.

6.9.4 Criteria for the termination of the trial.

6.9.5 Procedure for accounting for missing, unused, and spurious data.

6.9.6 Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).

6.9.7 The selection of subjects to be included in the analyses (e.g. all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).

6.10 Direct Access to Source Data/Documents

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

6.11 Quality Control and Quality Assurance

6.12 Ethics

Description of ethical considerations relating to the trial.

6.13 Data Hand ling and Record Keeping

6.14 Financing and Insurance

Financing and insurance if not addressed in a separate agreement.

6.15 Publication Policy

Publication policy, if not addressed in a separate agreement.

6.16 Supplements

(NOTE: Since the protocol and the clinical trial/study report are closely related, further relevant information can be found in the ICH Guideline for Structure and Content of Clinical Study Reports.)